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EXAMINER	
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ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,046	YOKOI ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26 and 31-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26 and 31-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner for this current application at the USPTO has changed. Examiner Samira Jean-Louis can be reached at 571-270-3503.

Response to Amendment

This Office Action is in response to the amendment submitted on 08/01/08. Claims 1-26 and 31-38 are currently pending in the application, with claims 27-30 having being cancelled. Accordingly, claims 1-26 and 31-38 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

However, given that applicant stated on the record upon entry of the 371 U.S. National application that the specification is a direct translation of the PCT, support for the term " sucrose fatty acid ester" cannot be found. Thus, the examiner concludes that applicant does not have priority to the PCT date, April 28, 2003. As for priority to the foreign document, JP2002-290367, it is noted that applicant has not provided English translation of the Japanese application as required by 35 U.S.C. 119(b). Without the English translation, one cannot ascertain if the instant invention is present in the Japanese application. Therefore, art prior to the PCT date and the foreign priority date of the Japanese application may be cited against the claims.

Alternatively, applicant may submit a certified English translation of the PCT or a declaration stating on the record that the PCT application was erroneously translated and the particular erroneous sections to be amended.

Applicant's argument with respect to the 112, second paragraph rejection has been fully considered and is not found persuasive. While applicant submitted a Pharmacopoeia Fifteen Edition to support applicant's arguments, the aforementioned document clearly indicates that the potency of cefditoren pivoxil can be expressed as mass of cefditoren. Nowhere in the document does it show that efficacy is synonymous to potency. In fact in the pharmacology art, efficacy is referred to as the ability of a drug to produce a functional response while potency is a measure of the concentrations of a drug at which it is effective. Moreover, applicant's claim of adding 0.1 to 100 mg of a sucrose fatty acid ester on the basis of an amount equivalent to 100 mg efficacy is indefinite as addition of any dosage of a non-active to obtain an amount equivalent to 100 mg efficacy of an active is highly unlikely. Consequently, the claims as presented are indeed indefinite and therefore the aforementioned rejection is maintained.

Applicant's contention that the Examiner has erroneously interpreted Shimizu as applicant's claims are directed to cefditoren pivoxil and a sucrose ester fatty acid and not a sugar ester fatty acid is acknowledged but is not found persuasive. The claims as previously presented recited the limitation of a pharmaceutical composition comprising amorphous cefditoren pivoxil and a sugar ester fatty acid. Shimizu et al. teach

disintegrable solid pharmaceutical preparations comprising a pharmacologically active including cefditoren pivoxil, with a hydroxypropylmethylcellulose, sugars, and additives including a sugar fatty acid ester such as Polysorbate 80 (i.e. sorbitan monooleate). Consequently, Shimizu does indeed render obvious applicant's invention. As for applicant's arguments that Shimizu et al. teach sugar and not a sugar fatty acid ester, such arguments are not persuasive as the Examiner did not state that the sugar referred to therein was a sugar fatty acid ester. Rather the Examiner points out that Shimizu teaches enteric coating of the cefditoren pivoxil granules (see pg. 33, table). Thus, the rejection of record was indeed proper.

Applicant's argument with respect to the examples in the original specification which showed improved amorphous maintenance period of time of the claimed invention has been fully considered but is not found persuasive. The examiner would again like to reiterate that applicant's arguments are directed to the newly added claims. It is further noted that the features upon which applicant relies (i.e., composition with an amorphousness-retaining character) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, applicant's arguments are rendered moot.

For the foregoing reasons, the rejections of record under 103 (a) were indeed proper. However, in view of applicant's amendment, the following 112, second paragraph and modified 103 (a) Final rejections are being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 2,5, and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (**see M.P.E.P 608.01 (k)**).

Claims 2, 5, and 9-11 are particularly vague and indefinite given that applicant is claiming 0.1 to 100 mg sucrose ester fatty acid on the basis of an equivalent to 100 mg efficacy of cefditoren pivoxil (see lines 2-3 of claims 2, 5, and 9-11). Given that applicant did not particularly point out what is meant by efficacy given that the art recognized term refers to concentration potency rather than efficacy, one of ordinary skill in the art would not be able to fully ascertain the metes and bounds of the aforementioned claims. Moreover, adding 0.1-100 mg of sucrose fatty acid ester on the basis of an amount which is equivalent to 100 mg efficacy of cefditoren pivoxil is highly unlikely as the sucrose fatty acid ester and the claimed compound possess contrasting pharmacological profiles and thus no amount of sucrose fatty acid ester would be equivalent to cefditoren pivoxil.

As a result of the above inconsistencies, the aforementioned claims are unable to be examined as disclosed given that the scope of the claimed subject matter would not be able to be determined by one of ordinary skill in the art. However, for the purpose of examination, Examiner will construe that the stated ranges set forth in the claims for the amount of sucrose fatty acid esters are the intended concentrations to be used in the aforementioned composition.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-26 and 31-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu et al. (WO00/06126, previously cited) and Onodera et al. (U.S. Patent 6,486,149, previously cited), and further in view of Hoffmann et al. (U.S. 2002/0015730 A1).

Shimizu et al. teach a rapidly disintegrable solid pharmaceutical preparation comprising a pharmacologically active ingredient of which the antibiotic, cefditoren pivoxil, is included within a Markush group (see p. 7, line 8); a polymer, for example, hydroxypropylmethylcellulose (see p. 12, line 25; p. 17, lines 18-20 and 27; and p. 32 Example 1, in Table corresponding to the "Undercoating Liquid"); and a sugar (see abstract and pg. 2, lines 5-9). Importantly, Shimizu et al. teaches addition of various additives including binders such as hydroxypropyl methyl cellulose and lubricants such as magnesium stearate and sucrose fatty acid ester (instant claims 1 and 20; see pg. 12, lines 24-25 and pg.13, line 25).

Applicant's invention also may further comprise a pharmaceutically acceptable polymer (claims 3-4, 7-8, 23-24) which is also represented as a water-soluble high polymer (claims 4, 8, and 24) and is hydroxypropylmethyl cellulose (claims 4, 7, and 23). Each of these additional limitations is also taught by Shimizu et al., in that the polymer-hydroxypropylmethyl cellulose is included in the undercoating liquid (see p. 32, lines 18-20). Further applicant's invention may also comprise one or more pharmaceutically acceptable additives (claims 6 and 12-19); which are likewise taught by Shimizu et al. as being included in the initial inner core which contains the pharmacologically active agent, as well as lactose, a well-established pharmaceutically acceptable excipient or the inclusion of crystalline cellulose (see pg. 15, lines 26-29, pg. 17, and pg. 19-20).

Applicant's pharmaceutical composition is further defined in that it comprises particles of cefditoren pivoxil present in an interior portion of said particles and a sugar

ester fatty acid present in an exterior portion of said particles (claim 20). In his description of Coating Method (see pg. 21), Shimizu et al. teach production of powders having a core in which the active pharmacological ingredient and the water-soluble polymer (i.e. hydroxypropyl methyl cellulose) are admixed wherein the concentration of the water-soluble polymer is 0.1-50% by weight of the composition (see pg. 21, lines 14-18, pg. 25, lines 5-10, 18-20, and 27-29, pg. 26, lines 8-13 and pg. 36, Spray Liquid). A second coating can also be made using a water-soluble polymer to obtain a composition (see pg. 23, lines 7-15, and pg. 32, Undercoating liquid, lines 18-20). Moreover, Schimizu et al. teach the use of a third coating (i.e. enteric coating) containing a sugar fatty acid ester (see pg. 33, Enteric film coating). Thus, in this example, the active pharmacological ingredient is the interior portion of the particles and the sugar fatty acid ester is located on the exterior portion of these particles. Similar to the pharmaceutical composition of claim 1, the composition of claim 20 also further comprises a pharmaceutically acceptable polymer (claim 23), which is hydroxypropylmethyl cellulose (claim 24). As stated above, these additional components are taught by Shimizu et al. (see p. 32, Tables for Spray liquid, lines 8-10 or Undercoating liquid, lines 18-20). Applicant further claims that the pharmaceutical may be produced as a tableted dose form (i.e. tablet) which is also disclosed by Shimizu et al. in section (7) production of orally disintegrable tablets that result in individual tablets each weighing 500 mg.

Applicant's invention further limits the amount of sugar ester fatty acid (0.1 mg-100 mg) or the amount of the polymer (1-100 mg) relative to the amount of cefditoren pivoxil (100 mg efficacy). The adjustment of particular conventional working conditions (e.g., determining result effective amounts of the ingredients beneficially taught by the cited reference, especially within the broad ranges instantly claimed), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. Accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Shimizu et al. do not teach amorphous cefditoren pivoxil or the particular sucrose fatty acid ester with an inherent property of the hydrophile-lipophile balance (HLB) value of 11-20.

Onodera et al. teach a process of making amorphous cefditoren pivoxil. Onodera et al. disclose that orthorhombic crystalline Cefditoren pivoxil had several advantages of high purity, high thermal stability and high storage stability, but that it was unsuitable for use in an oral dosage form due to its poor water solubility (see col. 2, lines 44-50). To overcome this poor water solubility, Onodera et al. teach that, "it is known that an amorphous substance generally has a high solubility in water, as compared with that of the corresponding crystalline substance" (see col. 2, lines 60-66). Onodera et al. further teach that an orally administrable amorphous and water soluble substance of Cefditoren pivoxil is obtained when Cefditoren pivaloyloxymethyl ester is homogenously mixed with

a water-soluble high-molecular additive such as a water- solubilized derivative of hydroxypropylmethyl cellulose and a pharmaceutically acceptable alkali metal salt or alkaline earth metal salt of an alginic acid ester of propylene glycol (see col. 3, lines 46-59; col. 6, lines 48-67 to col. 7, lines 1-43; col. 15 Example 2, wherein hydroxypropylmethyl cellulose is used; and Example 7 spanning col. 20-21). Because the amorphous Cefditoren pivoxil taught by Onodera et al. has about 10-fold greater water solubility (see results in Test Example 1, col. 27, lines 7-38 wherein the orthorhombic crystalline substance had a water solubility of about 0.4 mg/ml compared to the results of the compound obtained in Example 6 which had a water solubility of about 4 mg/ml); it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to employ the amorphous Cefditoren pivoxil taught by Onodera et al. into the pharmaceutical taught by Shimizu et al. in order to improve the water solubility of the cefditoren pivoxil and improve its overall absorption and efficacy.

Hoffmann et al. teach oral pharmaceutical formulation with variably adjustable release rate which comprises one or more active ingredients and one or more sucrose ester of a fatty acid as the sole release-controlling agent (see abstract and pg. 3, paragraph 0040). Hoffman et al. also teach the formulation in the form of a tablet wherein the sucrose esters of fatty acid are used in the range of 1-95% and are able to control the release of the active ingredients (see pg. 3, paragraphs 0042-0043, pg. 4, paragraphs 0059-0060). Importantly, Hoffman et al. teach the use of sucrose esters with a low HLB value from about 1 to about 16 (instant claims 21-22, 31, and 35; see

pg. 3, paragraph 0044-0045). Particularly, Hoffman et al. teach that the granules or pellets of the invention which may or may not contain sucrose esters of fatty acids in the granulate can be coated instead with sucrose fatty acid esters (instant claim 20; see pgs. 4-5, paragraphs 0061 and 0073).

Thus the pharmaceutical composition as taught by Shimizu et al. further meets Applicant's limitations to use of a sugar ester fatty acid with an HLB value of greater than 10 (claim 21) and also wherein the sugar ester fatty acid has an HLB value within the range of 11-20. Because Hoffman discloses that sucrose fatty acid esters with a value of greater than 10 can be used to control the release of pharmaceutical active ingredients; therefore, each and every limitation of claims 21 and 22 are met by the pharmaceutical composition taught by Shimizu et al. in view of Onodera and Hoffman.

It would have been obvious at the time of applicant's invention to one of ordinary skill in the art to select cefditoren pivoxil from the Markush group listing on p.7 and employ the coating techniques found in Example 1, substituting cefditoren pivoxil for the Lansoprazole would be reasonably expected to achieve a predictable result as that described in Example 1. Moreover, one of ordinary skill in the art would have found it obvious to substitute sucrose fatty acid esters of HLB greater than 10 for Polysorbate 80 since Hoffman et al. teach the use of such sucrose as controlled release agent with the reasonable expectation of providing a composition that is effective in releasing cefditoren pivoxil at particular site and appropriate time.

Regarding the limitation of the pharmaceutical composition retaining an amorphousness character for at least one day recited in claims 33-34 and 37-38, it is considered that one of ordinary skill in the art at the time of the invention was made would have found it obvious to conclude that the composition of Shimizu would possess the same amorphousness characteristic as that disclosed by the applicant given that these characteristics are obtained as a result of mixing the pharmaceutically active ingredient with a sugar fatty acid ester. Given that Shimizu et al. teach addition of lubricants such as sucrose ester fatty acid to the pharmaceutical active, the pharmaceutical composition of Shimizu would necessarily possess an amorphousness retaining character comparable to applicant's invention.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

11/13/2008

/Shengjun Wang/

Primary Examiner, Art Unit 1617